Original Article

ALPHA-FETOPROTIEN AS A DIAGNOSTIC TOOL IN DIFFERNTIATING HEPATOCELLULAR CARCINOMA FROM BENIGN HEPATIC DISORDERS

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ABSTRACT

OBJECTIVE: Differential diagnosis of hepatocellular carcinoma (HCC) from benign lesions of the liver is often difficult yet of great clinical importance. In the present study, we analysed diagnostic value of alpha-fetoproteins in hepato- cellular carcinoma.
DESIGN: A descriptive study
SETTING: Department of Internal Medicine, Liaquat University Hospital, Jamshoro, Sindh from February 2000 to December 2002.
SUBJECTS AND METHODS: Total 200 persons were studied. 100 presented with liver mass and other symptoms directing toward liver pathology, later confirmed histopathologically, as suffering from HCC while the other 100 subjects came to the department with jaundice and were HbsAg and anti-HCV positive on blood screening. All these subjects underwent blood test for alpha-fetoprotien. This tumor marker was analyzed by using enzyme immunoassay-based kit.
RESULTS: The alpha-fetoprotien positivity was statistically evaluated. In HCC, this test was statistically significant with p value of <0.001. In this study sensitivity of alpha-fetoprotien was 72%, specificity 89%, positive predictive value 86.7% and negative predictive value of 76.1%.
CONCLUSION: These findings suggest that alpha-fetoprotien has the potential to differentiate between benign and malignant liver diseases and it is a useful tool in the diagnosis of HCC.

KEY WORDS: ***Alpha-fetoprotiens. Hepatocellular carcinoma. Hepatitis B virus. Hepatitis C virus.***

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most severe sequelae of chronic liver disease. In spite of recent therapeutic advances, this malignancy continues to be a significant cause of cancer related morbidity and mortality in Asian and Western countries.[1] Surgical resection remains the treatment of choice for these tumours. Unfortunately, only 10-20% of primary liver tumours are found to be resectable at the time of diagnosis.[2] This cancer is still fatal in our country. So there is a need for detecting this disease at an early stage when the chances of treatment success are great.[3]

Thirty-five years after its description, alpha-fetoprotien still remains the gold standard tumor marker for liver cancer.[4] Serum level above the reference range of 10mg/ml occurs in approximately 75% of HCC patients.[5] Diagnostic accuracy along with alpha-fetoprotein can be further enhanced by other tests like ultrasound or CT scan. In the present study, we assessed the value of alpha-fetoprotien as a diagnostic tool which can be further useful to highlight HCC at an early stage due to its devastating effects at a later stage.

PATIENTS AND METHODS

The present study was carried out from February 2000 to December 2002 in the department of Internal Medicine, Liaquat University Hospital Jamshoro, Sindh. Among 200 persons studied, 100 were those who presented with liver mass or other symptoms directing towards liver pathology and were later diagnosed/confirmed histopathologically as suffering from HCC, the other 100 persons were those who came to the department with jaundice, and found HbsAg and anti-HCV positive on blood screening. All these subjects underwent blood test for alpha-fetoprotien. This tumor marker was analyzed by using enzyme immuno- assay based kit. The alpha-fetoprotien value of $\geq$ 8.6 ng/ml was taken as positive while less than it was taken as negative. From the positive and negative test reports, statistical value of this test was assessed. In this study p-value of alpha-fetoprotien was calculated.

RESULTS

The age range was 20-65 years with mean of 42.2 years of HCC patients and for HbsAg and anti-HCV positive patients, it was 18-54 years with mean of 37.3 years. Out of the liver cancer patients, 72 were positive for alpha-fetoprotein (i.e. with elevated levels than normal) and from HbsAg and anti-HCV positive patients, 11 were positive for alpha-fetoprotein as shown in **Table I**. Thus it was positive with statatical value of $p<0.001$ in significantly higher number of HCC patients as compared with HbsAg and anti-HCV positive subjects. The sensitivity of alpha-fetoprotien in this study is presented in **Table II.**

TABLE I: OUTCOME OF ALPHA-FETOPROTEIN TEST (n=200)

Criteria	Test positive	Test Negative	Total
Liver Cancer Patients	72	28	100
HbsAg and anti-HCV + Patients	11	89	100
Total	83	117	200

TABLE II: SENSITIVITY, SPECIFICITY, POSITIVE AND NEGATIVE PREDICTIVE VALUES OF ALPHA-FETOPROTEIN IN PATIENTS WITH HCC

Criteria	Result
Sensitivity	72%
Specificity	89%
Positive predictive value	86.7%
Negative predictive value	76.1%

DISCUSSION

An ideal biological marker or tumor marker should be highly sensitive and specific for a particular tumor to increase its diagnostic accuracy.[6] In these circumstances, a simple test would lend itself to screening and early diagnosis of cancer.[7] Until two decades ago, patients with HCC presented almost with advanced cancers that were incurable and for which there was no palliative therapy.[4,8] Recent advances in detection, sugery, chronic carrier state of HBV and vaccination have changed the picture positively.[9] HCC is the main histopathological subtype of primary liver cancer (PLC). This is eighth most frequent occurring cancer in the world, and the sixth among males.[10] With respect to cancer mortality, PLC ranks even higher as the fourth most common cause of death worldwide and the third among males due to its nearly uniform fatality.[11] Moreover, 77% of all PLC cases and deaths occur in the countries of developing world, where facilities for its detection and management are meagre.[10] In such countries, liver cancer are the seventh most frequent malignancy with the third highest number of deaths.[11] About 20-30% of chronic HBV carriers develops cirrhosis and 3% of cirrhotic patients develop HCC each year.[12] In this way cirrhosis of the liver can be regarded as a pre-malignant state since more that 80% of HCC in Western world result in a cirrhotic liver.[12] In a study from Hong Kong, more than 80% of cirrhotic patients were positive for HbsAg, which is 4-5 times higher than the developed world.[13] The role of hepatitis C virus (HCV) in hepato-carcinogenisis is similar to that of the HBV. Tumor progression and growth enhancement is through the pathogenesis of cirrhosis.[14-18] However, in most populations of the world, 0.5-2% of individuals have serological evidence of past or current HCV infection.[19] HCV has been suggested to be a causative factor for HCC in Japan and Europe. Infectivity with any or both the viruses should also be the consideration for HCC screening. Although HCC is common in Asia and Africa, the benefit of early diagnosis is still too low to be cost effective, but as positive HBsAg is very high in endemic areas, it is appropriate to consider screening of chronic hepatitis B carriers selectively. Alpha-fetoprotien can be used as a good screening tool in such patient population for HCC. Serum level above the reference range of 10 ng/ml occurs in approximately 75% of cases of HCC.[5] In one study, serum alpha-fetoprotien was elevated in 80% of patients with hepatocellular carcinoma at the time of presentation.[20] All patients with at-risk disorders should be considered for screening. In most cases, this means screening those with cirrhosis, especially when HBV, HCV, ethanol or alpha 1 anti trypsin deficiency is present. In a study, serum alpha-fetoprotein was a readily available screening test, with a sensitivity of 30-79% and a specificity 76-89%.[4] One study done in Pakistan showed sensitivity of 92.9% and specificity of 87.5% for alpha-fetoprotien.[21] As seen in our cases, the sensitivity, specificity, positive predictive value and negative predictive values are all

suggestive of diagnostic value of this tumor marker. In patients with HCC, 68% will have an alpha-fetoprotien >15 ng/ml and 36% will have >200 ng/ml as determined by one study.[4] In another study, alpha-fetoprotien at a high cut-off value of 100ng/ml showed highest sensitivity and specificity in detecting liver metastasis.[22] The presence or absence of alpha-fetoprotien in blood is a predictor of outcome in patients with HCC. Those with positive alpha-fetoprotien are more prone for extra-hepatic metastasis.[23] In one study alpha-fetoprotien level >100 ng/ml was seen in more than 70% of HCC cases while alpha-fetoprotien values higher than normal were found in most of the remaining cases of same study.[23] This study showed that alpha-fetoprotein was a useful diagnostic tool in the diagnosis of HCC. Since the HCC is increasing in our country and the majority presents in advanced stage while the intervention is not usually successful, hence, there is a need to screen and highlight this tumor at an early stage so that something can be done with a greater success.

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